

REMARKS**A. Status of the Claims**

Prior to the submission of this paper, claims 44-68, 70-76 and 78-85 were under examination and were rejected under one or more of 35 U.S.C. §§103(a) and 112. With this amendment, claims 71 and 79 have been cancelled without prejudice or disclaimer. When these claim cancellations have been entered, the claims under examination will be claims 44-68, 70, 72-76, 78 and 80-85.

Claims 44-67, 71, 74, 75, 79, 82- 85 are rejected under 35 U.S.C. § 112, ¶ 1 for alleged lack of enablement. According to the Examiner, the specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims.

Claims 70 and 78 are rejected under 35 U.S.C. § 112, ¶ 2 for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 82 is rejected under 35 U.S.C. § 112, ¶ 2, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 44-67 are rejected under 35 U.S.C. § 103(a) for allegedly being unpatentable over Fossel (U.S. Patent No. 5,895,658) ("Fossel") in view of Cooke et al. (U.S. Patent No. 6,605,115 B1) ("Cooke"), in further view of Rothbard et al. (U.S. Patent Application Publication No. 2002/0009491) ("Rothbard").

Claims 68, 70, 76, and 78 are rejected under 35 U.S.C. § 103(a) for allegedly being unpatentable over Fossel, in view of Cooke and in further view of Rothbard.

Claims 72 and 80 are rejected under 35 U.S.C. § 103(a) for allegedly being unpatentable over Fossel, in view of Cooke and Rothbard and in further view of Frome (U.S. Patent No. 5,571,794) (“Frome”).

Claims 71, 74, 79, 82, 84 and 85 are rejected under 35 U.S.C. § 103(a) for allegedly being unpatentable over Fossel, in view of Cooke and Rothbard, and in further view of Gazzani (U.S. Patent No. 5,053,230) (“Gazzani”).

Claims 73 and 81 are rejected under 35 U.S.C. § 103(a) for allegedly being unpatentable over Fossel, in view of Cooke and Rothbard as applied to claims 68, 70, 76 and 78 and in further view of Kligman (U.S. Patent No. 4,877,805) (“Kligman”).

B. Explanation of Amendments

Claims 44 and 56 have been amended to replace the phrase “wherein the cosmetic formulation does not contain a therapeutic agent that is delivered by the polymer” with the phrase “wherein the polymer does not deliver any other therapeutic agent.” Basis for these amendments can be found in paragraph [0012] of U.S. Pre-Grant Publication No. 20050226821, which states that “the present invention is directed to the use of arginine oligomers as prophylactic or therapeutic/cosmeceutical agents in their own right...”.

Claim 62 has been amended to remove the word “and” before the phrase “or hair colorant.”

Claims 68 and 76 have been amended to remove the phrase “wherein the cosmetic effect is not promotion of hair regrowth.”

Claims 74 and 82 have been amended to recite “amelioration of fat atrophy or fat regression in the skin.” Support for this amendment can be found at least at the last paragraph of page 9 of the original specification, which states that

[t]he compositions of the present invention may also be used for stabilization or remodeling of hypodermal or deeper fat. Fat stabilization, particularly in humans, is generally associated with the appearance of aging attributed to fat atrophy as well as fat regression in the skin. The methods and compositions described herein can assist in preventing the formation of wrinkles and aid in ameliorating the appearance of deep wrinkles by supporting vascularity of the skin.

Claims 75 and 83 have been amended to specify that the cosmetic effect is a “transient enlargement of gums”. Support for this amendment is found in paragraph 3 of the originally filed specification.

Claims 84 and 85 have been amended to depend from claims 68 and 76, respectively. Furthermore, Applicant’s have cancelled some of the species of the Markush groups recited in claims 84 and 85. The cancellation of this subject matter is made without prejudice or disclaimer, and Applicant hereby reserves the right to file claims directed to the cancelled subject matter in a later application.

Applicant respectfully submits that no new matter is added by these amendments.

C. Rejections under 35 U.S.C. §112, ¶ 1 (Enablement)

1. Claims 44-67 Are Enabled

The Examiner asserts that claims 44-67 are not enabled over the full scope of the claimed invention, stating that “if the claims are read broadly, the polymer cannot be a therapeutic agent because the polymer can not contain a therapeutic agent” [Office Action, page 5 (emphasis in the original)]. The Examiner further notes that “[t]he specification does not enable the separation of a polymer being a delivery agent and a therapeutic agent.” [Office Action, page 5].

In view of these passages in the Office Action, it appears that the rejection is based on the portions of claims 44 and 56 which state that “the cosmetic formulation does not contain a therapeutic agent that is delivered by the polymer.” The Examiner apparently takes the position that the polymer inherently can act as both a delivery agent and a therapeutic agent, and that delivery of the polymer inherently delivers a therapeutic agent as well.

Applicant respectfully requests reconsideration and withdrawal of this rejection, in view of the amendments to independent claims 44 and 56, which now specify that the “the polymer does not deliver any other therapeutic agent.” This claim language clearly acknowledges the inherent therapeutic benefit of the polymer and is consistent with paragraph [0012] of the originally filed specification, which discloses that arginine oligomers can function as prophylactic or therapeutic/cosmeceutical agents in their own right.

2. Claims 74 and 82 Are Enabled

The Examiner rejects claims 74 and under 35 U.S.C. § 112, ¶ 1 for allegedly lacking enablement. While the Examiner acknowledges that the specification enables treatment of wrinkles, the Examiner takes the position that the specification “does not enable the treatment of all conditions that would benefit from the stabilization or remodeling of fat.” [Office Action, p. 10].

Without agreeing to the propriety of the rejection, Applicant respectfully requests reconsideration and withdrawal of the rejection in view of the amendments to claims 74 and 82. As amended, claims 74 and 82 specify that the claimed method is directed to amelioration of fat atrophy or fat regression in the skin. Support for this amendment appears at least at the last paragraph of page 9 of the original specification.

3. Claims 71, 79, 84 and 85 Are Enabled

The Examiner rejects claims 71, 79, 84 and 85 under 35 U.S.C. § 112, ¶ 1 for allegedly lacking enablement. According to the Examiner, the specification, "while being enabling for alleviating textural discontinuities of the skin, loss of firmness, loss of skin tightness and loss of skin recoil, does not reasonably provide enablement for alleviating all signs of aging, particularly discoloration, blotching, sallowness, hyperpigmented skin regions, keratoses, abnormal differentiation, hyperkeratinization, elastosis, collagen breakdown of skin, and histological changes in the stratum corneum, dermis, epidermis, and skin vascular system." [Office Action, p. 12].

Without agreeing to the propriety of the rejection, Applicant respectfully requests reconsideration and withdrawal of the rejection in view of the cancellation of claims 71 and 79 and the amendments to claims 84 and 85. The cancellation of the subject matter in claims 84 and 85 are made without prejudice or disclaimer, and Applicants hereby reserve the right to pursue the subject matter cancelled from claims 84 and 85 in a later filed continuation application.

4. Claims 75 and 83 Are Enabled

The Examiner rejects claims 75 and 83 under 35 U.S.C. §112, ¶1 for allegedly lacking enablement. The Examiner states that "[t]he specification as filed does not speak on or show any working examples [or] any studies performed that treats gum regression with the claimed compound by means of dilating blood vessels (i.e. vasodilation) of the gum" [Office Action, p. 19, ¶6]. Furthermore, the Examiner contends that the prior has established that vasodilation actually

exacerbates gum disease, citing U.S. Patent 5,922,766 to Chan (“Chan”). According to the Examiner, Chan teaches that excess nitric oxide, which is a vasodilator, contributes to chronic inflammation, which is associated with periodontitis. On this basis, the Examiner states that one of ordinary skill in the art would not want to provide a vasodilator to treat gum regression [Office Action, p. 19].

Applicants respectfully traverse the rejection. As an initial matter, Applicants note that the Examiner’s statements with respect to Chan, if anything, support the patentability of the claims by establishing that the prior art teaches away from the use of a vasodilator, such as the presently claimed arginine polymers, to mitigate the effects of gum regression. Moreover, claims 75 and 83 have been amended to clarify that the cosmetic benefit is “a transient enlargement of gums”. Thus, the present claims are directed to a transient cosmetic alteration of the appearance of the treated gums, rather than to a cure that addresses the root causes of the gum regression. These amendments are supported by Applicants’ specification, which states that vasodilation may be used to achieve a cosmetic benefit, even if gum regression itself is incurable:

[a]dditionally, structures such as gums regress with age and with inappropriate care (hard toothbrush bristles, etc). This regression is still thought to be irreversible. However, the appearance might be mitigated by vasodilatation for at least a transient cosmetic benefit. (Paragraph [0003], emphasis added).

In view of the foregoing remarks and amendments to the claims, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

D. Rejections under 35 U.S.C. §112, ¶ 2 (Indefiniteness)1. Claims 70 and 78 Are Not Indefinite

The Examiner rejects claims 70 and 78 under 35 U.S.C. § 112, ¶ 2, contending that they are indefinite, because they are inconsistent with their respective independent claims (claims 68 and 76). Specifically the Examiner notes that claims 68 and 76 specify that the claimed cosmetic effect is not promotion of hair regrowth, whereas claims 70 and 78 specify that the cosmetic effect is promotion of hair growth and treatment of hair loss.

In response, Applicants have amended claims 68 and 76 to remove the phrase “wherein the cosmetic effect is not promotion of hair regrowth.” Accordingly, Applicants respectfully request withdrawal of the indefiniteness rejection of claims 70 and 78.

2. Claim 82 Is Not Indefinite

The Examiner rejects claim 82 under 35 U.S.C. § 112, ¶ 2 for allegedly being indefinite, noting that there appeared to be missing text from the end of the claim. Claim 82 has been amended to supply the missing text. Support this amendment is found in Applicants’ originally filed specification at the last paragraph of page 9.

In light of the above, Applicants respectfully request withdrawal of these rejections under 35 U.S.C. §112, ¶ 2.

E. Claims 44-67 Are Patentable Over the Cited References

Applicants respectfully traverse the rejection of claims 44-67 for allegedly being unpatentable over Fossel, in view of Cooke and Rothbard. The traversal is based on at least the following observations: (1) both Fossel and Cooke teach away from the claimed invention; and (2)

the proposed combination of references impermissibly changes the principle of operation of both Cooke and Rothbard. Accordingly, the rejection of claims 44-67 under 35 U.S.C. §103(a) should be withdrawn.

1. Fossel and Cooke Teach Away from the Claimed Invention

A prior art reference that teaches away from a claimed invention is an important factor to be considered in determining whether the claimed invention is obvious. In re Gurley 27 F.3d 551, 553 (Fed. Cir. 1994). “A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant.” Id. For example, “[a] reference teaches away if it leaves the impression that the product would not have the property sought by the applicant” In re Caldwell, 319 F.2d 254, 256, 138 USPQ 243, 245 (CCPA1963).

Cooke teaches away from the claimed invention. As Applicants noted in their previous response, Cooke reports that only in situations of “vascular injury” or trauma, where local L-arginine concentrations are depleted, would the supplementation of extracellular arginine polymers be expected to increase NO synthesis [Cooke, col. 9, lines 48-58]. In the absence of “vascular injury” or trauma, Cooke explicitly states that NO synthesis is “not dependent on extracellular supplementation” of arginine polymers because there is already an abundance of intracellular L-arginine:

Because intracellular levels of L-arginine normally greatly exceed the K_m of the NOS enzyme, NO synthesis is ordinarily not dependent on extracellular supplementation. However, under certain circumstances, local L-arginine concentration can become rate-limiting. Such

circumstances include elevated plasma or tissue levels of the endogenous NO synthase antagonist ADMA (asymmetric dimethylarginine) and inflammation-induced expression of the inducible NO synthase (iNOS). Both of these abnormalities are operative in the setting of vascular injury. [Cooke, col. 9, lines 48-58 (emphasis added)].

These statements of Cooke would not have led one of ordinary skill in the art to create a cosmetic composition comprising L-arginine polymers as recited in the present claims. To the contrary, one of ordinary skill in the art would have predicted, based on Cooke's specification, that no vasodilation effect would be observed when L-arginine polymers are applied for cosmetic purposes, because no vascular injury or trauma is involved in such applications. Thus, Cooke teaches away from the present invention, because it suggests that L-arginine polymers would not cause vasodilation if used for cosmetic purposes. See Caldwell at 256 (stating that "[a] reference teaches away if it leaves the impression that the product would not have the property sought by the applicant").

Fossel also teaches away from the claimed invention. Fossel reports that the high charge density of free L-arginine molecules (i.e., monomers) makes the free monomer resistant to transfer into the tissue. Accordingly, Fossel requires the inclusion of agents having high ionic strength (choline chloride, magnesium chloride and sodium chloride) to "create a biophysically hostile environment in the delivery vehicle such that L-arginine would prefer to be in tissue, or to package L-arginine in such a way that it is carried into tissue or neutralize its charge by derivitization or forming a neutral salt." (See Fossel, Abstract and col. 3, line 39 through col. 4, line 9). Because L-arginine polymers are even more highly charged than L-arginine monomers, Fossel discourages the skilled artisan from topically applying L-arginine polymers for cosmetic purposes, by suggesting that the penetration ability of L-arginine polymers would be expected to be quite low.

Since two of the three references relied upon by the Office Action to reject claims 44-67 for being obvious *actually teach away* from the claimed invention, the rejection of claims 44-67 under 35 U.S.C. §103(a) is improper and should be withdrawn. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 44-67.

2. The Office Action Impermissibly Changes the
Principle of Operation of both Cooke and Rothbard

A proposed modification of the prior art may not change the principle of operation of the prior art invention being modified. If it does, then the teachings of the prior art reference are not sufficient to render the claims *prima facie* obvious. In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959) (holding that a claimed invention that required *resiliency* of a particular component was not obvious over a reference that required *rigidity*).

Here, the Office Action proposes to change the principle of operation of two of the three references that it relies upon in its attempt to establish obviousness. Cooke uses L-arginine polymers exclusively for preventing the migration and proliferation of smooth muscle cells in the vasculature, which may result from trauma caused by surgery [Cooke, col. 3, lines 10-40]. To achieve this effect, Cooke teaches that the L-arginine polymers should be directly applied to the vascular tissue, typically via a surgical procedure. For example, Cooke states that

after a necrotic vessel segment (lesion) has been removed (transected), the remaining vascular region downstream from the excision site (distal to the heart) is clamped at a point several centimeters (e.g., 4 cm) from the proximal end of the downstream (distal) region, the clamped region is filled with arginine polymer solution, and the proximal end is then clamped to create a "sausage" containing the polymer solution. After the arginine polymer solution has been incubated in the clamped region for an appropriate time, the proximal clamp is removed, and the arginine polymer solution is optionally removed, followed by removal of

the remaining clamp. [Cooke, col. 14, lines 17-29 (emphasis added)].

Notwithstanding these teachings by Cooke to apply L-arginine polymers to internal tissues (vasculature) for the purpose of reducing unwanted cell proliferation, the Office Action contends that it would have been obvious to apply L-arginine polymers to external tissues (e.g., the skin) for the purpose of achieving a cosmetic effect resulting from vasodilation. However, this attempt to establish obviousness fails, because the Office Action's proposed modification of Cooke completely changes Cooke's principle of operation, including the route of administration of the L-arginine polymers and the condition to be treated.

The Office Action's proposed modification also completely changes the principle of operation of Rothbard. As Applicants noted in the previous response, Rothbard is directed to the use of charged polymers, such as polyarginine, for the delivery of therapeutic agents. Nowhere does Rothbard teach or suggest the use of arginine polymers, in and of themselves, for the purpose of achieve a beneficial effect, such as the cosmetic effects recited in Applicants' specification and claims. Thus, the Office Action proposed use of Rothbard's polyarginine is inconsistent with Rothbard's teachings to use polyarginine as a delivery agent, and therefore improperly changes the principle of operation of Rothbard.

For these reasons as well, the Office Action's reliance on Cooke and Rothbard is improper and the rejection of claims 44-67 under 35 U.S.C. §103(a) should be withdrawn.

F. Applicants Claims Are Patentable Over Fossel, Cooke, and Rothbard, in view of the Cited Quaternary References.

Applicants respectfully traverse the rejection of claims 68, 70, 76, and 78 over Rossel, Cooke, and Rothbard; the rejection of claims 72 and 80 over Fossel, Cooke, Rothbard, and Frome; the rejection of claims 71, 74, 79, 82, and 84 over Fossel, Cooke, Rothbard, and Gazzani; and the rejection of claims 73 and 81 over Fossel, Cooke, Rothbard and Kligman.

As discussed above, the Office Action's reliance on Fossel, Cooke, and Rothbard is misplaced, because (1) Fossel and Cooke teach away from the claimed invention; and (2) the Office Action's proposed modification of these references improperly changes the principle of operation of both Cooke and Rothbard. The addition of a fourth reference (e.g., Frome, Gazzani, or Kligman) does not change the fact that Fossel and Cooke teach away from the claimed invention or that the Office Action's proposed modifications to Cooke and Rothbard are improper.

Accordingly, Applicants respectfully maintain that these rejections under 35 U.S.C. §103(a) should be withdrawn. Applicants respectfully request reconsideration and withdrawal of these grounds of rejection.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. 50-3732, Order No. 13720-105110.

Respectfully submitted,
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